EXHIBIT 1

OIPE IAP15 MAR 06 2006 PATENT & TRADEMARK OFFICE

GENP.001C1

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Brown et al.
Appl. No.	:	09/931,732
Filed	:	August 16, 2001
For	:	ANTISENSE OLIGONUCLEOTIDES COMPRISING UNIVERSAL AND/OR DEGENERATE BASES
Examiner	:	Jon Benjamin Ashen
Group Art Unit	:	1635

DECLARATION UNDER 37 CFR §1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I declare and state as follows:

1. I am an inventor of the invention claimed in the above-captioned patent application.

2. During the time period in which I participated in the events and activities described herein, I was employed by Oasis Biosciences, Inc., the prior assignee of the above-captioned application, who has assigned its rights to the present assignee, Gen-Probe Incorporated.

3. All of the events and activities described herein were performed by me personally, or by others at my direction as part of my duties as an employee of Oasis Biosciences, Inc.

4. The subject matter and utility of the claimed invention in the above-captioned patent application was conceived prior to March 25, 1999 and diligently reduced to practice thereafter in the U.S. as described below.

5. Prior to March 25, 1999, I and/or my co-inventors conceived of the invention claimed in the above-captioned patent application. For example, prior March 25, 1999, the idea of down-regulating multiple allelic variants of the same gene differing by single nucleotide polymorphisms (SNPs) with a single oligonucleotide, was conceived. Thus, conception of the invention claimed in the above-captioned patent application occurred prior to March 25, 1999.

Appl. No. : **09/931,732**
Filed : **August 16, 2001**

6. As evidence of conception of, among others, down-regulating multiple allelic variants of the same gene differing by several SNPs, with a single oligonucleotide prior to March 25, 1999, submitted herewith as Exhibit A is a copy of a communication from me to the attorney preparing the priority documents of the present patent application, U.S. Provisional Application 60/128,377, prior to March 25, 1999. Exhibit A details, for example, down-regulating multiple allelic variants of the same gene differing by several SNPs, with a single oligonucleotide.

7. Thereafter, filing of the U.S. Provisional Application was diligently pursued, and U.S. Provisional Application 60/128,377 was filed on April 8, 1999.

8. I hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

By: Bob D. Brown
Bob D. Brown, Ph.D.

Date: Nov. 1st, 2006

EXHIBIT A

Fax Message

4 pages

Please Deliver To:
Neil Bartfeld
Knobbe, Martens
619-235-0176 Fax

From: Oasis Biosciences Inc.
3550 General Atomics Ct.
Bldg 2 Suite 343
San Diego, CA 92121
619-455-4600
619-455-4605 fax

RE: Gene examples for Universal Base patent.

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Example: Down regulating multiple alleles of the same gene

Comparison of allelic variations in an important human oncogene, bcl-2, reveals several single nucleotide polymorphisms (SNPs) within the general human population. Over expression of any known allele of bcl-2 have been shown to confer chemoresistance in human tumors and is regarded as a poor prognostic indicator.

Two or more alleles of the bcl-2 gene can be targeted with single oligonucleotides containing universal or ambiguous bases without restriction by occurrence of SNPs, as shown below.

Human bcl-2B mRNA (HUMBCL2B) GenBank #M13995 versus
Human bcl-2C mRNA (HUMBCL2C) GenBank #M14745.
Base numbers are as defined in GenBank.

```
bcl-2B: 116 gttggccccgttgcttttcctctgggaaggatggcgcacgctgggagaacggggtacga 175
            |||||||||||||*|||||||||||||||**|||||||||||||||||||*||||||||
bcl-2C: 1   gttggccccgttacttttcctctgggaaatatggcgcacgctgggagaacagggtacga 60

bcl-2B: 176 caaccgggagatagtgatgaagtacatccattataagctgtcgcagaggggctacgagtg 235
            *|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
bcl-2C: 61  taaccgggagatagtgatgaagtacatccattataagctgtcgcagaggggctacgagtg 120

bcl-2B: 236 ggatgcgggagatgtgggcgccgcgcccccgggggccgcccccgcaccgggcatcttctc 295
            ||||||||||||||||||||||||||||||||||||||||||||*||||||||||||||
bcl-2C: 121 ggatgcgggagatgtgggcgccgcgcccccgggggccgcccccgcgccgggcatcttctc 180

bcl-2B: 296 ctcccagcccgggcacacgccccatccagccgcatcccgcgacccggtcgccaggacctc 355
            |||*|||||||||||||||||||*||||||||||||*||||||||||||||||||||
bcl-2C: 181 ctcgcagcccgggcacacgccccatacagccgcatcccgggacccggtcgccaggacctc 240

bcl-2B: 356 gccgctgcagaccccggctgccccggcgccgccgcggggcctgcgctcagcccggtgcc 415
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
bcl-2C: 241 gccgctgcagaccccggctgccccggcgccgccgcggggcctgcgctcagcccggtgcc 300

bcl-2B: 416 acctgtggtccacctggccctccgccaagccggcgacgacttctcccgccgctaccgcgg 475
            ||||||||||||||||*|||||||||*||||||||||||||||||||||||||||*||
bcl-2C: 301 acctgtggtccacctgaccctccgccaggccggcgacgacttctcccgccgctaccgccg 360

bcl-2B: 476 cgacttcgccgagatgtccagccagctgcacctgacgcccttcaccgcgcggggacgctt 535
            ||||||||||||||||||||*||||||||||||||||||||||||||||||||||||||
bcl-2C: 361 cgacttcgccgagatgtccaggcagctgcacctgacgcccttcaccgcgcggggacgctt 420
```

Example: Down regulating distantly related homologous genes

Bcl-2A and bcl-xL are distantly related anti-apoptosis, transforming oncogenes and are over expressed in many human cancers. Most importantly, the over expression

of bcl-2 family members (typically bcl-2A) or bcl-xL has been shown to confer chemoresistance to cells.

Previously reported attempts (unpublished) to knockout both genes simultaneously have been based on conventional oligonucleotides that are perfectly complimentary to one gene or the other, but not both, and thus have several mismatches and low activity against one of the target genes. Thus, these early attempts have relied on non-specific RNase H-dependent activity of long oligonucleotides.

Simultaneous knockout of these two oncogenes can be accomplished with a single oligonucleotide containing one or more universal or ambiguous bases targeted to the small region of high nucleotide homology found between the genes, as shown below.

Human bcl-2A mRNA (HUMBCL2A) GenBank #M13994 versus
Human bcl-xL mRNA (HSBCLXL) GenBank #Z23115

Asterisks indicate mismatches in the region of nucleotide homology. Base numbers are as defined in GenBank.

```
bcl-2A: 2020 tggatccaggataacggaggctgggatgcctttgtggaact 2060
             ||||||||||*||||||*||||||||||*|*||||||||||
bcl-xL: 675  tggatccaggagaacggcggctgggatacttttgtggaact 715
```

Sample 20mer antisense oligonucleotides (typical of antisense oligonucleotides in common use) complimentary to the region of overlap shown above:

5′ CCACAAAKGPATCCCAGCCBCCGTTBTCC 3′

5′ AGTTCCACAAAKGPATCCCA 3′ covers bases 2060 to 2041 in bcl-2A and bases 715 to 696 in bcl-xL.

5′ CAAAKGPATCCCAGCCBCCG 3′ covers bases 2053 to 2034 in bcl-2A and bases 708 to 689 in bcl-xL.

5′ CCCAGCCBCCGTTBTCCTGG 3′ covers bases 2044 to 2025 in bcl-2A and bases 699 to 680 in bcl-xL.

Sample 13mer antisense oligonucleotides (short by conventional standards) complimentary to the region of overlap shown above:

5′ KGPATCCCAGCCB 3′ covers bases 2049 to 2037 in bcl-2A and bases 704 to 692 in bcl-xL.

5′ CCACAAAKGPATC 3′ covers bases 2056 to 2044 in bcl-2A and bases 711 to 699 in bcl-xL.

Example: Down regulating two or more related genes

The Protein Kinase C (PKC) gene family consists related protein products that regulate cell growth by phosphorylating other proteins in response to extracellular signals. Over expression of PKC genes has been detected in several human tumor types and PKC genes are believed to be potential cancer therapy targets.

In spite of the similarity of PKC family members at the protein level, the nucleotide sequences can be significantly different. Antisense oligonucleotides containing universal or ambiguous bases offer a way to simultaneously target two or more PKC family members at the nucleotide level.

Human Protein Kinase C Alpha mRNA (PKCa, HSPKCA1), GenBank #X52479 versus
Human Protein Kinase C Theta mRNA (PKCt, HUMPKCTH), GenBank # L07032 versus
Human Protein Kinase C Delta mRNA (PKCd, HUMPCKD13X) GenBank # L07860.
Base numbers are as defined in GenBank.

Homology region one (PKCa, PKCt, PKCd):

```
alpha: 1276 atggaatatgtcaacggtggggacctcatgtaccacat 1313
            ||||| |   ||||||| |||||| | ||||||||||
theta: 1393 atggagtacctcaacggaggggacttaatgtaccacat 1430
            ||||| |   ||||||| |||||| | ||||||
delta: 1337 atggagttcctcaacgggggggacctgatgtac 1369
```

Homology region two (PKCa, PKCt, PKCd):

```
alpha: 1398 aggaatcatttatagggatctgaagttagataacgtcatgttggattcagaaggacatat 1457
            || ||  | || ||||| || ||  | || ||  |  |||| ||    || || || ||
theta: 1515 aggaatagtctacagggacctgaagctagataacatcctgttagacaaagatggacatat 1574
            || ||  | || ||||| || ||  | || ||  |  |||| ||    || || || ||
delta: 1459 gggcatcatttacagggacctcaaactggacaatgtgctgttggaccgggatggccacat 1518

alpha: 1458 caaaattgctgactttgggatgtgcaaggaacacatgatggatggagtcacgaccaggac 1517
            ||| || || || ||||| |||||||| ||  |||| | | |    | | | |  ||
theta: 1575 caagatcgcggattttggaatgtgcaaggagaacatgttaggagatgccaagacgaatac 1634
            ||| || || || ||||| |||||||| ||  |||| | | |    | | | |  ||
delta: 1519 caagattgccgactttgggatgtgcaaagagaacatattcggggagagccgggccagcac 1578

alpha: 1518 cttctgtgggactccagattatatcgccccagagat 1553
            |||||| || || || || || |||||||| |||||
theta: 1635 cttctgtgggacacctgactacatcgccccagagat 1670
            |||||| || || || || || |||||||| |||||
delta: 1550 cttctgcggcacccctgactatatcgcccctgagat 1614
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